

10/ 614481 09/ 07/ 2006

Connecting via Wnsock to Dialog

Logging in to Dialog

Trying 31060000009998... Open

DIALOG INFORMATION SERVICES
PLEASE LOGON:

ENTER PASSWORD:

Welcome to DIALOG

Dialog Level 05.22.00D

Last Logoff: 25nov08 09:01:45
Logon file405 02dec08 14:57:44
*** ANNOUNCEMENTS ***

*** Join us for Update 2008! Dialog is holding updates this fall in several areas and would love for you to join us. Visit www.dialog.com/events/update to register or enter HELP UPDATES for more information.

*** "Thomson File Histories" are now available directly through Dialog in selected patent and trademark files. Combined with the comprehensive patent and trademark information on Dialog, file histories give you the most complete view of a patent or trademark and its history in one place. When searching in one of the patent and trademark databases, a link to an online order form is displayed in your search results, saving you time in obtaining the file histories you need. See HELP FILEHOST for more information about how to use the link and a list of files that contain the link.

NEW FILE
*** File 651, TRADEMARKSCAN(R) - China. See HELP NEWS 651 for details.
RESUMED UPDATING
*** File 523, D&B European Financial Records

RELOADS COMPLETED
*** File 227, TRADEMARKSCAN(R) - Community Trademarks

FILES RENAMED
*** File 321, PLASPEC now known as Plastic Properties Database

FILES REMOVED
*** File 601, Early Edition on Canada

>>>For the latest news about Dialog products, services, content <<<
>>>and events, please visit What's New from Dialog at <<<
>>><http://www.dialog.com/whatsnew/>. You can find news about <<<
>>>a specific database by entering HELP NEWS <file number>. <<<
>>>PROFILE is in a suspended state.
>>>Contact Dialog Customer Services to re-activate it.
* * *

SYSTEM HOME
Cost is in Dial Units
Menu System 11: D2 version 1.8.0 term=ASCII
*** DIALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DIALOG(R) Document Delivery
7. DataStar(R)

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/H = Help /L = Logoff /NOVENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERICO).
? b 410

02dec08 14:57:44 User 217743 Session D745.1

10/ 614481 09/ 07/ 2006

```
$0.00 0.271 Dial Units FileHomeBase
$0.00 Estimated cost FileHomeBase
$0.00 Estimated cost this search
$0.00 Estimated total session cost 0.271 Dial Units
```

File 410: Dialog Comm -of -Interest Newsletters 2008 / Mar
(c) 2008 Dialog

Set	Items	Description
? set hi ;set hi		
Hi Li GHT set on as ''		
Hi Li GHT set on as ''		
? b 411		
02dec08 14: 57: 48 User 217743 Session D745. 2		
\$0.00 0.115 Dial Units File410		
\$0.00 Estimated cost File410		
\$0.02 TELNET		
\$0.02 Estimated cost this search		
\$0.02 Estimated total session cost 0.386 Dial Units		

File 411: DI ALI INDEX(R)

DI ALI INDEX(R)
(c) 2008 Dialog

```
*** DI ALI INDEX search results display in an abbreviated ***
*** format unless you enter the SET DETAILED CN command. ***
? set files bi ochem
You have 29 files in your file list.
(To see banners, use SHOW FILES command)
? s IL()6 and crp and cancer
```

Your SELECT statement is:
s IL()6 and crp and cancer

Items	File
133	5: Bi osis Previ ews(R) _1926- 2008/ Nov W4
17	24: CSA Li fe Sci ences Abstr acts _1966- 2008/ Nov W4
176	34: Sci Search(R) Cited Ref Sci _1990- 2008/ Nov W4
31	45: EMCar e_2008/ Nov W4
15	50: CAB Abstr acts _1972- 2008/ Nov W5
112	71: ELSEVIE R BI OBASE_1994- 2008/ Nov W8
206	72: EMBASE_1993- 2008/ Dec 02
211	73: EMBASE_1974- 2008/ Dec 01
1	76: Env i ronment al Sci ences_1966- 2008/ Nov W4
3	98: General Sci Abs_1984- 2008/ Oct
84	144: Pascal_1973- 2008/ Nov W5
130	154: MEDLI NE(R) _1990- 2008/ Nov 24
130	155: MEDLI NE(R) _1950- 2008/ Nov 24
14	156: ToxFi le_1965- 2008/ Nov W2
28	162: Gl obal Health_1983- 2008/ Nov W5
7	172: EMBASE Al ert_2008/ Nov 27
7	399: CA SEARCH(R) _1967- 2008/ UD=14922

17 files have one or more items; file list includes 29 files.

? b 155
02dec08 14: 59: 03 User 217743 Session D745. 3
\$9.29 3.161 Dial Units File411
\$9.29 Estimated cost File411
\$0.53 TELNET
\$9.82 Estimated cost this search
\$9.84 Estimated total session cost 3.546 Dial Units

File 155: MEDLI NE(R) _1950- 2008/ Nov 24
(c) format only 2008 Dialog

* File 155: NLM has suspended updating from 11/ 20- 24/ 2008, as it begins preparations for the annual reload.

Set	Items	Description
? s IL()6 and crp and cancer		
171027	IL	
2142376	6	
37229	IL(W6	
14333	CRP	
667774	CANCER	
S1 130	IL()6 AND CRP AND CANCER	
? s IL()6/ti and crp and cancer		
53893	IL/ TI	
97606	6/ TI	
4003	IL/ TI (W6/ TI	
14333	CRP	

667774 CANCER
S2 10 IL()6/TI AND CRP AND CANCER
? t s2/3, ab/ all

2/ 3, AB/ 1
DI ALOG(R) File 155: MEDLINE(R)
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28156761 PM D: 18844497
Serum interleukin-6 (IL-6) and C-reactive protein (CRP)
Levels in colorectal adenoma and cancer patients.
Grobelska Magdalena; Moczko Barbara; Wereszczynska-Siemiatowska
Urszula; Kedra Boguslaw; Lukaszewicz Marta; Banickiewicz Andrzej;
Szmitkowski Maciej
Department of Biochemical Diagnostics, Medical University, Białystok,
Poland.

Clinical chemistry and laboratory medicine - CCLM / FESCC (Germany)
2008; 46 (10) p1423-8, ISSN 1434-6621 - Print Journal Code: 9806306

Publising Model Print
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process

BACKGROUND: Colorectal cancer is one of the most common cancers of the gastrointestinal tract and the fourth cause of cancer death in the world. It has been shown that local chronic inflammation may lead to colorectal carcinogenesis via adenomatous polyps. Interleukin-6 and C-reactive protein are biomarkers of inflammation and indicators of the immune response to tumors. **METHODS:** Serum levels of interleukin-6, carcinoembryonic antigen and carbohydrate antigen 19-9 were determined using immunoenzymatic assays, and C-reactive protein concentrations by immunoturbidimetric kits in 76 colorectal cancer patients before surgery, in 38 colorectal adenoma patients and in 35 healthy controls. **RESULTS:** Serum levels of interleukin-6, C-reactive protein and carcinoembryonic antigen were significantly higher in cancer patients when compared to adenoma patients and healthy subjects, and increased in more advanced stages of disease and in patients with non-resectable tumors. Based on Cox's analysis, the elevated preoperative serum level of C-reactive protein was an independent significant prognostic factor for patients' survival. **CONCLUSIONS:** Our findings suggest the usefulness of interleukin-6 in the diagnosis of colorectal cancer patients and C-reactive protein in the survival prognosis.

2/ 3, AB/ 2
DI ALOG(R) File 155: MEDLINE(R)
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16437355 PM D: 15955385
Relationship of obesity and visceral adiposity with serum concentrations of CRP, TNF-alpha and IL-6.
Park Hye Soon; Park Jung Yul; Yu Ri na
Department of Family Medicine, Asan Medical Center, University of Ulsan
College of Medicine, 388-1 Pungnap-dong, Songpa-gu, Seoul 138-736, South Korea, hyesoon@amc.seoul.kr

Diabetes research and clinical practice (Ireland) Jul 2005; 69 (1)
p29-35, ISSN 0168-8227 - Print Journal Code: 8508335
Publising Model Print-Electronic
Document type: Journal Article; Research Support, Non-U.S. Gov't
Languages: ENGLISH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

OBJECTIVE: To investigate the relationship between serum concentrations of the cytokines C-reactive protein (CRP), tumor necrosis factor (TNF)-alpha, and interleukin (IL)-6, and obesity and visceral adiposity. **METHODS:** A cross-sectional study of 100 Korean adults free from pre-existing inflammatory disease or cancer was performed. Body mass index (BM), waist circumference, and serum concentrations of CRP, TNF-alpha and IL-6 were measured. In 46 obese subjects, fat mass was assessed by bioimpedance analysis and abdominal fat distribution was determined by computerized tomography scan. **RESULTS:** Overall, serum concentrations of CRP, TNF-alpha and IL-6 were significantly correlated with weight, BM, waist circumference, hip circumference, and waist-hip ratio. In obese subjects, CRP and IL-6 were significantly correlated with BM, waist circumference and visceral adipose tissue. Multiple regression analysis showed that CRP was significantly associated with BM, whereas IL-6 was significantly related with visceral adiposity in obese subjects. **CONCLUSIONS:** The positive associations of obesity and visceral adiposity with elevated cytokine levels suggest the importance of reducing obesity and visceral adiposity to prevent elevations in cytokine levels.

DI ALOG(R) File 155: MEDLINE(R)
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16300615 PM D: 15786541

Serum IL-6, TNFalpha and CRP levels in Greek colorectal cancer patients: prognostic implications.

Nikiteas Nikolas; Tzanakis Nikolas; Gazouli Maria; Pallis George; Daniilidis Kessaris; Theodoropoulos George; Kostakis Alkiviadis; Peros George

2nd Propedeutic Department of Surgery, School of Medicine, University of Athens, Athens 11527, Greece. nnikit@med.uoa.gr

World Journal of Gastroenterology - WJG (China) Mar 21 2005, 11 (11) p1639-43, ISSN 1007-9327--Print Journal Code: 100883448

Publication Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Complete

AIM The significance of preoperative serum IL-6, TNFalpha and CRP levels in the progression of colorectal cancer (CRC) has not been fully elucidated. Our intention was to investigate their role and identify their prognostic significance. METHODS: The IL-6, TNFalpha and CRP levels were measured in 74 CRC patients and the relationships between their elevations and both the clinicopathological factors and prognosis of patients were investigated. Serum concentrations of human IL-6 and TNFalpha were determined by enzyme-linked immunosorbent assay (ELISA). CRP was measured by an immunoturbidometric method. RESULTS: Median IL-6, TNFalpha and CRP levels were significantly higher in CRC patients than in normal controls. High levels of serum IL-6, TNFalpha and CRP were correlated with larger tumor size. Furthermore, high IL-6 and high CRP levels were associated with reduced overall survival. CONCLUSION: Serum IL-6, TNFalpha and CRP levels definitely increase in CRC patients. Pre-operative serum elevation of IL-6 and CRP was thus found to be predictor of the prognosis of CRC patients. The clinical value of TNFalpha in CRC needs to be further investigated.

2/3, AB/4

DI ALOG(R) File 155: MEDLINE(R)

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15916569 PM D: 15309885

C-reactive protein as a prognostic variable that reflects uncontrolled up-regulation of the IL-1-IL-6 network system in colorectal carcinoma.

Miki Chiako; Konishi Naomi; Oshima Eiki; Hatada Tsuyoshi; Inoue Yasuhiro; Kusunoki Masato

Second Department of Surgery, Mie University School of Medicine, Mie, Japan.

Digestive Diseases and Sciences (United States) Jun 2004, 49 (6)

p970-6, ISSN 0163-2116--Print Journal Code: 7902782

Publication Model Print

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: MEDLINE; Complete

Up-regulation of the IL-1-IL-6 network stimulates systemic expression of C-reactive protein (CRP). This cytokine network system plays a pivotal role in inducing angiogenic growth factors in intestinal mucosa. Serum CRP level and tissue concentrations of cytokines in colorectal cancer patients were determined and an *in vitro* model was employed to determine the time course of induction of IL-6 in Caco-2 cells. Increased serum CRP was associated with recurrent disease and shorter survival time. Intense surgical stress and the presence of an acute phase reactant were independently associated with overexpression of IL-6 in the tumor. Enhanced IL-6 protein expression in Caco-2 cells induced by the initial treatment with IL-1beta or lipopolysaccharide could be abrogated by additional supplementation of IL-1ra. The presence of an acute phase reactant reflects uncontrolled up-regulation of the local IL-1-IL-6 network system in the tumor, which may enhance the survival and proliferation of remnant cancer cells after tumor resection.

2/3, AB/5

DI ALOG(R) File 155: MEDLINE(R)

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15552321 PM D: 14654926

Association of serum IL-6 levels with comprehensive geriatric assessment variables in a population of elderly cancer patients.

Mantovani Giovanni; Madeddu Clelia; Gramignano Giulia; Ferrelli Luca; Massa Elena; Contu Paolo; Serpe Roberto

Department of Medical Oncology, University of Cagliari, Italy. mantovan@acs.unica.it

Oncology reports (Greece) Jan 2004, 11 (1) p197-206, ISSN 1021-335X
--Print Journal Code: 9422756
Publishing Model Print
Document type: Journal Article
Languages: ENGLISCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed

The primary aim of this study was to find whether any association exists between serum levels of proinflammatory cytokines, mainly IL-6, and the most important comprehensive geriatric assessment (CGA) variables such as functional status, cognitive functions and nutrition in a population of elderly cancer patients. The secondary aims were to find whether any difference existed between: i) age groups, ii) performance status scores, iii) patients who had lost weight versus those who had not. Eighty-four elderly patients with advanced cancer were included in the study (stage III 15.4% and stage IV 72.6%). Serum levels of IL-6 and CRP were significantly higher in elderly than in the other adult cancer patients. Among the CGA variables investigated, the most affected were functional status assessed by IADL, cognitive functions by MMSE and nutrition. The ECOG PS was shown to be significantly associated with all the dimensions of CGA investigated: poor PS ($>/=2$) corresponded to severe disabilities. As for the relationship of serum IL-6 with CGA variables, the strongest correlations were between IL-6 and functional status assessed by both Katz ADL ($p=0.0003$), IADL ($p=0.0070$) and nutrition ($p=0.0013$). Moreover, we observed an association, although not statistically significant, between functional disability (ADL and IADL) and high IL-6 levels in individuals with weight loss. IL-6 levels seem to be independently associated with all CGA variables investigated in the present study in a population of elderly cancer patients. Because the most important CGA variables, in particular functional status, have been observed to be strongly associated with survival, the present study, confirming our previously reported ones, suggests that IL-6 may be a reliable marker of disease outcome and supports the feasibility of using IL-6 as a sensitive outcome marker in studies based on novel approaches aiming at modifying age- and cancer-related biological mechanisms.

2/ 3, AB/ 6
DI ALOG(R) File 155: MEDLINE(R)
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15446964 PM D: 14599731
Relationship of total and abdominal adiposity with CRP and IL-6 in women.
Rexrode Kathryn M; Pradhan Aruna; Manson Joann E; Buring Julie E; Ridker Paul M
Center of Cardiovascular Disease Prevention, Division of Preventive Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02215, USA. krexrode@partners.org
Annals of Epidemiology (United States) Nov 2003, 13 (10) p674-82,
ISSN 1047-2797 - Print Journal Code: 9100013
Contract/Grant No.: CA-47988; CA; United States NCI; HL-43851; HL; United States NHLBI
Publishing Model Print

Document type: Journal Article; Research Support, U.S. Gov't, P.H.S.
Languages: ENGLISCH
Main Citation Owner: NLM
Record type: MEDLINE; Completed
PURPOSE: To examine the relationship between different measures of adiposity as predictors of C-reactive protein (CRP) and interleukin-6 (IL-6) levels. METHODS: A cross-sectional study of 733 women free from preexisting cardiovascular disease or cancer at baseline. MEASUREMENTS: Total adiposity, as measured by body mass index (BM). Abdominal adiposity, as measured by waist circumference (WC) and waist/hip ratio (WHR). High sensitivity CRP levels and IL-6 levels. RESULTS: BM, WHR, and WC were all significantly correlated with CRP and IL-6, throughout the anthropometric spectrum. After adjustment for risk factors, the odds ratios (ORs) were 12.2 (95% CI, 6.44-23.0) for elevated CRP ($>/=75$ th percentile) and 4.13 (95% CI, 2.37-7.18) for elevated IL-6 ($>/=75$ th percentile) in comparisons of extreme BM quartiles. Among women in the highest WC quartile, the OR for elevated CRP and IL-6 were 8.57 (95% CI, 4.59-16.0) and 4.40 (95% CI, 2.46-7.89), while ORs for the highest WHR quartile were 2.88 (95% CI, 1.60-5.19) and 1.76 (95% CI, 1.03-3.01), respectively. Compared with lean nonusers, women in the highest BM quartile who did not use hormone therapy (HT) had an OR for elevated CRP of 7.79 (95% CI, 2.08-29.2) vs. 31.6 (95% CI, 7.97-125.6) for current hormone users. CONCLUSIONS: Indices of both total and abdominal adiposity were strongly associated with significant increased levels of CRP and IL-6. This association was evident across the entire spectrum of BM.

2/ 3, AB/ 7
DI ALOG(R) File 155: MEDLINE(R)

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13552360 PM D: 10769674

TNF al pha, IL-1 bet a and IL-6 production by peripheral bl ood monocytes in patients with renal cell carcinoma.

Ikemoto S; Sugimura K; Yoshida N; Wada S; Yamamoto K; Kishimoto T
Department of Urology, Osaka City University Medical School, Japan.
Anti cancer research (GREECE) Jan-Feb 2000, 20 (1A) p317-21, ISSN 0250-7005- Print Journal Code: 8102988

Publ i shing Model Print

Document type: Comparative Study; Journal Article

Languages: ENGLI SH

Main Citation Owner: NLM

Record type: MEDLI NE; Compl eted

Renal cell carcinoma (RCC) has been shown to be immunologically more labile than other types of cancer. In this study, we examined tumor necrosis factor al pha (TNF al pha), interleukin-1 bet a (IL-1 bet a) and interleukin-6 (IL-6) production of peripheral bl ood monocytes in 38 RCC patients. Monocytes were isolated from peripheral bl ood mononuclear cells by adherence to a plastic dish and cultured with lipopolysaccharide for 24 hours. The culture supernatant was obtained, and the production of TNF al pha, IL-1 bet a and IL-6 was measured by ELISA. As a result, TNF al pha and IL-1 bet a production was significantly higher in the high stage patients compared to the control subjects and low stage patients. When the patients were divided according to serum C-reactive protein (CRP), TNF al pha, IL-1 bet a and IL-6 production was significantly higher in the CRP-positive patients compared to the control subjects and the CRP-negative patients. Overexpression of these cytokines may therefore induce a hypermetabolic status that may be a cause of malnutrition and cancer cachexia.

2/ 3, AB/ 8

DI ALOG(R) File 155: MEDLI NE(R)

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13549669 PM D: 10768866

Effect of IL-6 elevation in malignant pleural effusion on hyperfibrinogenemia in lung cancer patients.

Yamaguchi T; Kimura H; Yokota S; Yamamoto Y; Hashimoto T; Nakagawa M; Ito M; Ogura T

Department of Internal Medicine, Toneyama National Hospital, Osaka, Japan.

Japanese journal of clinical oncology (JAPAN) Feb 2000, 30 (2) p53-8
ISSN 0368-2811- Print Journal Code: 0313225

Publ i shing Model Print

Document type: Journal Article; Research Support, Non-U.S. Gov't

Languages: ENGLI SH

Main Citation Owner: NLM

Record type: MEDLI NE; Compl eted

BACKGROUND: The involvements of interleukin-6 (IL-6) and fibrinogen in cancer development were elucidated independently, irrespective of IL-6 activity to induce fibrinogen. This study was undertaken to clarify the clinical pathological association of these molecules in lung cancer patients with malignant pleurisy. METHODS: IL-6, fibrinogen and the related molecules in blood and pleural effusion of 38 patients were assayed at 3-day intervals. RESULTS: IL-6 levels were elevated in sera of 27 cases (71.1%) and in all the effusions with mean values of 20.5 and 9970.5 pg/ml, respectively. Their correlation in 22 cases who were examined on the same day was statistically strong ($r = 0.902$, $p < 0.0001$). Occasional elevations of tumor necrosis factor-al pha were independent of IL-6 elevation. Levels of plasma fibrinogen, fibrin(ogen) degradation products (FDP) and C-reactive protein (CRP) were more frequently elevated in the IL-6 elevated cases than those without IL-6 elevation. In all pleural effusions, fibrinogen levels were significantly decreased to <150 mg/dl with large elevations of FDP level. Immunologically, IL-6 was detected in cancer cells in 16 cases of adenocarcinoma in addition to host pleural cells, but its cellular positivity was not reflected in the IL-6 level in each pleural effusion. CONCLUSION: Compared with lung cancer patients without malignant pleurisy, IL-6, fibrinogen, FDP and CRP levels in patients with malignant pleurisy were increased more frequently in their peripheral blood. These were basically attributed to systemic leakage of IL-6 from the affected pleural cavity, in which plasma fibrinogen induced in response to serum IL-6 was exudated and degraded predominantly to FDP.

2/ 3, AB/ 9

DI ALOG(R) File 155: MEDLI NE(R)

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13536952 PM D: 10749586

CRP, TNF- al pha, IL-1ra, IL-6, IL-8 and IL-10 in bl ood serum of col orectal cancer patients.

Kamińska J; Kowalska M M Nowacki M P; Chwalinski M G Rysińska A; Fuksi ewicz M
Maria-Sklodowska-Curie Memorial Cancer Centre and Institute of Oncology,
Department of Tumor Markers, Roentgen 5, Warsaw, 02-781, Poland.
Pathology oncology research - POR (HUNGARY) 2000, 6 (1) p38-41,
ISSN 1219-4956 - Print Journal Code: 9706087

Publ i shing Model Print
Document type: Comparative Study; Journal Article

Languages: ENGLI SH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

Blood serum cytokines: TNFalpha, IL-1ra, IL-6, IL-8, IL-10 as well as CRP were investigated in patients with colorectal cancer, prior treatment and 1, 10 and 42 days after surgery. There was an increase of the levels of CRP, IL-6 and IL-10 in most patients 24 hours after surgery. The levels of IL-1ra were elevated in patients in stage C and in several patients in stage B of the disease and there was a decrease of circulating TNFalpha in stage B patients. On day 10 and 42 after surgery, the levels of cytokines followed various patterns.

2/3, AB/10
DI ALOG(R) File 155: MEDLINE(R)
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11495814 PM D: 7579407

Measurement of whole body interleukin-6 (IL-6) production:
prediction of the efficacy of anti-IL-6 treatments.

Lu Z Y; Brailly H; Wijdenes J; Bataille R; Rossi J F; Klein B
Institute for Molecular Genetics, CNRS BP5051, Montpellier, France.
Blood (UNITED STATES) Oct 15 1995, 86 (8) p3123-31, ISSN 0006-4971
-- Print Journal Code: 7603509

Publ i shing Model Print

Document type: Clinical Trial; Journal Article

Languages: ENGLI SH

Main Citation Owner: NLM

Record type: MEDLINE; Completed

A major limitation on the therapeutic use of cytokine antagonists is that the amount of cytokine to be neutralized *in vivo* is not presently known. We previously reported that anti-interleukin-6 (IL-6) monoclonal antibody (mAb) administered to a patient with multiple myeloma (MM) induced high amounts of IL-6 to circulate in the form of monomeric immune complexes. Based on this observation, the present study developed a new methodology to estimate daily IL-6 production in 13 patients with MM or renal cancer who received anti-IL-6 mAb. Treatment was considered effective when the production of C-reactive protein (CRP) was inhibited. The production of this acute-phase protein by hepatocytes is dependent on the activation of IL-6 gp130 transducer. Inhibition of tumor proliferation was also evaluated in patients with MM. In 7 of 13 patients whose CRP production was completely inhibited (> 96%) and who showed some antitumoral effects, whole-body IL-6 production *in vivo* was less than 18 micrograms/d (median, 5.7 micrograms/d; range, 0.5 to 17.5 micrograms/d). In the other 6 patients, subtotal inhibition of CRP production and a lack of antitumoral response were associated with high IL-6 production (median, 180 micrograms/d; range, 18 to 358 micrograms/d). These *in vivo* observations were consistent with mathematical modeling that predicted that anti-IL-6 mAb treatment would be efficient only in low IL-6 producers. These data indicate the difficulty of neutralizing IL-6 with a single anti-IL-6 mAb *in vivo* and call for new strategies to avoid accumulation of IL-6 in the form of stable immune complexes.

? logout

>>> invalid set number

? logout

02dec08 15:01:43 User 217743 Session D745.4

\$4.03 1.146 Dial Units File155

\$2.40 10 Type(s) in Format 4 (UDF)

\$2.40 10 Types

\$6.43 Estimated cost File155

\$0.80 TELNET

\$7.23 Estimated cost this search

\$17.07 Estimated total session cost 4.692 Dial Units

Logoff: Level 05.22.00 D 15:01:43

Connecting via Winsock to Dialog

Logging in to Dialog

Trying 31060000009998... Open

DI ALOG INFORMATION SERVICES
PLEASE LOGON:

10/ 614481 09/ 07/ 2006

ENTER PASSWORD:

Welcome to DI ALOG

Dialog Level 05.22.00D

Last Logoff: 02dec08 15:01:43
Logon file405 02dec08 15:16:53
>>>PROFILE is in a suspended state.
>>>Contact Dialog Customer Services to re-activate it.

SYSTEM HOME

Cost is in Dialog Units

Menu System II: D2 version 1.8.0 term=ASCII
*** DI ALOG HOMEBASE(SM) Main Menu ***

Information:

1. Announcements (new files, reloads, etc.)
2. Database, Rates, & Command Descriptions
3. Help in Choosing Databases for Your Topic
4. Customer Services (telephone assistance, training, seminars, etc.)
5. Product Descriptions

Connections:

6. DI ALOG(R) Document Delivery
7. Data Star (R)

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/H = Help

/L = Logoff

/NOVENU = Command Mode

Enter an option number to view information or to connect to an online service. Enter a BEGIN command plus a file number to search a database (e.g., B1 for ERIC).
? b 410

02dec08 15:16:54 User 217743 Session D746.1
\$0.00 0.267 Dialog Units FileHomeBase
\$0.00 Estimated cost FileHomeBase
\$0.00 Estimated cost this search
\$0.00 Estimated total session cost 0.267 Dialog Units

File 410: Dialog Comm-of-Interest Newsletters 2008 / Mar
(c) 2008 Dialog

Set	Items	Description
? set hi ;set hi		
HI LI GHT	set on as ''	
HI LI GHT	set on as ''	
? b 155		
02dec08 15:16:58 User 217743 Session D746.2		
\$0.00 0.117 Dialog Units File410		
\$0.00 Estimated cost File410		
\$0.02 TELNET		
\$0.02 Estimated cost this search		
\$0.02 Estimated total session cost 0.384 Dialog Units		

File 155: MEDLINE(R) 1950-2008/ Nov 24

(c) format only 2008 Dialog

* File 155: NLM has suspended updating from 11/20-24/2008, as it begins preparations for the annual reload.

Set	Items	Description
? s (reduce or reduction) adj2 inflammatory adj markers		
>>> Invalid syntax		
? s (reduce or reduction) with inflammatory() markers		
>>> Invalid syntax		
? s (reduce or reduction) and inflammatory() markers		
230294 REDUCE		
569508 REDUCTI ON		
310015 INFLAMMATORY		
295160 MARKERS		
3397 INFLAMMATORY(W MARKERS		
S1 428 (REDUCE OR REDUCTI ON) AND INFLAMMATORY() MARKERS		
? s s1 and c() reactive() protein		
428 S1		
1207816 C		
167884 REACTI VE		
1863179 PROTEI N		
25278 C(W REACTI VE(W PROTEI N		

S2	206	S1 AND C() REACTI VE() PROTEI N
? s s2 and IL() 6	206	S2
171027	IL	
2142376	6	
37229	IL(W 6	
S3	56	S2 AND IL() 6
? s s3 and il() 6/ti	56	S3
53893	IL/TI	
97606	6/TI	
4003	IL/TI (W 6/TI	
S4	0	S3 AND IL() 6/TI
? s s2/ti	S5	S2/TI
? s s3 and s5	56	S3
86	S5	
S6	25	S3 AND S5
? t s6/ti , ab/al		

6/ TI , AB/ 1

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Interleukin-6 is a better predictor of mortality as compared to C-reactive protein, homocysteine, pentosidine and advanced oxidation protein products in hemodialysis patients.

Inflammatory markers predict mortality in hemodialysis (HD) patients, whereas a possible association between oxidative stress (OS) markers and survival is less clear. We assessed the impact on all-cause mortality of baseline inflammatory [high-sensitivity C-reactive protein and interleukin-6 (IL-6)] and OS markers (advanced oxidation protein products, pentosidine, homocysteine) in 112 HD patients. We found no significant correlations between inflammatory and OS markers. During the 5.5 years of follow-up, 51 patients died. In a Kaplan-Meier analysis, the survival rate was reduced in patients with IL-6 higher than the median (IL-6 >4.2 pg/ml) (log-rank = 6.47; p = 0.01), in diabetics (log-rank = 12.26; p = 0.0005) and in older patients (log-rank = 11.22; p = 0.0008). Moreover, in Cox analysis only IL-6 and age were independently associated with mortality. We conclude that in this group of prevalent Brazilian HD patients, IL-6 was a better predictor of survival than other inflammatory and OS markers. Copyright 2008 S. Karger AG, Basel.

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Effect of psyllium fiber supplementation on C-reactive protein: the trial to reduce inflammatory markers (TRIM).

PURPOSE: Recent evidence supports a significant association between the intake of dietary fiber and levels of inflammatory markers. The objective of this study was to determine whether daily fiber supplementation would reduce levels of inflammatory markers. **METHODS:** This study was a prospective randomized controlled trial at a single university medical center. Participants were overweight or obese adults with no history of heart disease. The intervention was psyllium supplementation at either 7 or 14 g/d for 3 months compared with no supplements in a control group. The main outcome measure was change in level of high-sensitivity C-reactive protein (hsCRP) concentration; secondary outcomes included changes in interleukin-6 (IL-6) levels, fibrinogen levels, and white blood cell (WBC) count. Protocol completers attended at least 2 visits and took more than 75% of the prescribed fiber dose. **RESULTS:** In this intent-to-treat analysis (n = 158), there were no significant differences between either of the 2 treatment groups and the control group in the amount of change in CRP, fibrinogen, or IL-6 levels or in WBC count (P>.05). In the analysis of protocol completers (n = 132), there also were no significant differences between the groups except for a small decrease in fibrinogen level in the high-fiber group (-6 mg/dL [-0.18 micromol/L] compared with 13 mg/dL [0.38 micromol/L] in the control group, P<.05). **CONCLUSION:** Psyllium fiber supplementation did not significantly reduce CRP levels in overweight or obese individuals in this trial, and changes in other markers were not consistent. Further research is needed to determine whether other fibers or nutrients can reduce inflammatory markers.

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Xuezhi Kang, an extract of cholestain, decreases plasma inflammatory markers and endothelin-1, improve exercise-induced ischemia and subjective feelings in patients with cardiac syndrome X.

Previous studies have demonstrated that Xuezhi keng, an extract of cholestin, available from Chinese red yeast rice, could effectively modify lipid profile. The present study was undertaken to investigate whether Xuezhi keng could modify endothelin-1 (ET-1), interleukin-6 (IL-6), high-sensitivity C-reactive protein (CRP) and exercise-induced ischaemia in patients with cardiac syndrome X (CSX). Thirty-six patients with CSX were randomly assigned to 1200 mg/d of Xuezhi keng or placebo group (n=18 respectively). Blood samples were drawn at day 0 and day 90 for measuring above parameters. The treadmill exercise tests and subjective feelings were also assessed at day 0 and day 90. The data showed that Xuezhi keng therapy resulted in significant reductions in total cholesterol (TC, 19%, low-density lipoprotein cholesterol (LDL-C) (26%), and triglycerides (TG) compared with baseline (16% $p<0.01$ respectively). The data also showed that Xuezhi keng led significantly to reductions in median and log-CRP levels (38% and 44% $p<0.01$ respectively), IL-6 (20% $p<0.01$), and ET-1 (47% $p<0.01$) compared with baseline. The exercise duration, and time to 1 mm ST-segment depression was significantly prolonged after Xuezhi keng therapy (9% and 6% $p<0.05$ respectively) accompanied by improvement of subjective feelings. Data suggested that the benefit of Xuezhi keng resulted in significant modification of vascular function by reduction of ET-1, inflammatory markers and LDL cholesterol, which may be clinically important for patients with CSX.

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Effect of tiotropium on sputum and serum inflammatory markers and exacerbations in COPD.

Chronic obstructive pulmonary disease (COPD) patients experiencing frequent exacerbations demonstrate increased stable-state airway inflammation. Tiotropium has been shown to reduce exacerbation frequency, but its effect on airway inflammation is unknown. The aim of the present study was to investigate the effect of tiotropium on sputum inflammatory markers and exacerbation frequency. Patients (n = 142) were randomised to receive tiotropium or placebo in addition to their usual medication for 1 yr. Sputum and serum cytokines were assayed by ELISA and exacerbation frequency calculated using a symptom-based diary. There was no difference in the area under the curve for sputum interleukin (IL)-6 or myeloperoxidase between the groups, but sputum IL-8 level was increased in the tiotropium arm. There was no difference between start and end of study in serum IL-6 or C-reactive protein level. Tiotropium was associated with a 52% reduction in exacerbation frequency (1.17 versus 2.46 exacerbations.yr(-1)). Of patients on tiotropium 43% experienced at least one exacerbation, compared with 64% on placebo. The total number of exacerbation days was reduced compared with placebo (17.3 versus 34.5 days). Tiotropium reduces exacerbation frequency in chronic obstructive pulmonary disease, but this effect does not appear to be due to a reduction in airway or systemic inflammation.

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The effect of testosterone replacement therapy on adipocytokines and C-reactive protein in hypogonadal men with type 2 diabetes.

OBJECTIVE: Serum testosterone levels are known to inversely correlate with insulin sensitivity and obesity in men. Furthermore, there is evidence to suggest that testosterone replacement therapy reduces insulin resistance and visceral adiposity in type 2 diabetic men. Adipocytokines are hormones secreted by adipose tissue and contribute to insulin resistance. We examined the effects of testosterone replacement treatment on various adipocytokines and C-reactive protein (CRP) in type 2 diabetic men. DESIGN: Double-blinded placebo-controlled crossover study in 20 hypogonadal type 2 diabetic men. Patients were treated with testosterone (sustanon 200 mg) or placebo intramuscularly every 2 weeks for 3 months in random order followed by a washout period of 1 month before the alternate treatment phase. METHODS: Leptin, adiponectin, resistin, tumor necrosis factor-alpha (TNF-alpha), interleukin (IL)-6 and CRP levels were measured before and after each treatment phase. Body mass index (BM) and waist circumference were also recorded. RESULTS: At baseline, leptin levels significantly correlated with BM and waist circumference. There was a significant inverse correlation between baseline IL-6 and total testosterone ($r=-0.68$; $P=0.002$) and bioavailable testosterone levels ($r=-0.73$; $P=0.007$). CRP levels also correlated significantly with total testosterone levels ($r=-0.59$; $P=0.01$). Testosterone treatment reduced leptin (-7141.9 +/- 1461.8 pg/ml; $P=0.0001$) and adiponectin levels (-2075.8 +/- 852.3 ng/ml; $P=0.02$). There was a significant reduction in waist circumference. No significant effects of testosterone therapy on resistin, TNF-alpha, IL-6 or CRP levels were observed. CONCLUSION: Testosterone replacement treatment decreases leptin and adiponectin levels

in type 2 diabetic men. Moreover, low levels of testosterone in men are associated with pro-inflammatory profile, though testosterone treatment over 3 months had no effect on inflammatory markers.

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School-based intervention acutely improves insulin sensitivity and decreases inflammatory markers and body fatness in junior high school students.

CONTEXT: Risk factors for type 2 diabetes mellitus (T2DM) include obesity, family history, dyslipidemia, a proinflammatory state, impaired insulin secretory capacity, and insulin resistance. OBJECTIVE: The aim of this study was to examine the effects of a 3- to 4-month school-based intervention consisting of health, nutrition, and exercise classes plus an aerobic exercise program on diabetes risk. DESIGN: This study was a randomized before/after controlled trial. METHODS: Seventy-three eighth-grade students in a predominantly Hispanic New York City public school were divided into a control group (studied twice without receiving the intervention) and an experimental group (studied before and after the intervention). OUTCOME MEASURES: We measured body fatness (bioelectrical impedance), insulin sensitivity, beta-cell function (insulin release in response to an iv glucose load corrected for insulin sensitivity), lipid profiles, and circulating concentrations of IL-6, C-reactive protein, adiponectin, and TNF-alpha. RESULTS: Participation in the intervention was associated with significant reductions in body fatness, insulin resistance, and circulating concentrations of C-reactive protein and IL-6, irrespective of somatype on enrollment. CONCLUSION: Short-term school-based health, nutrition, and exercise intervention is beneficial to all students and affects multiple diabetes risk factors.

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The effects of short term (3 weeks) testosterone treatment on serum inflammatory markers in men undergoing coronary artery stenting.

OBJECTIVE: Inflammation markers can predict restenosis after successful intracoronary stenting. There is evidence that testosterone suppresses the expression of the inflammatory cytokines. We hypothesized that testosterone therapy after coronary stenting can reduce the inflammation markers.

METHODS: We selected 41 men with coronary artery disease who underwent successful stent implantation for a >70% diameter stenosis of a major coronary artery. Patients, who had stable angina and positive exercise test results, were recruited after diagnostic coronary angiography. Twenty-five men were treated with 3 doses of i.m. testosterone administration once a week for 3 weeks following diagnostic angiography. Sixteen patients were recruited as a control group and they received standard therapy. First venous blood samples were obtained after angiography. Stents were implanted 3 weeks after diagnostic angiography. Second venous blood samples were taken 24 h after the coronary stenting. RESULTS: Baseline biochemical or hematological parameters were similar between the control and treatment groups. After coronary stenting, free testosterone, total testosterone, and sex hormone binding globulin were significantly elevated in the testosterone group ($P<0.0001$, $P<0.0001$ and $P=0.02$; respectively). After coronary stent implantation, there was a significant increase in IL-6 and CRP levels in the control group only ($P=0.02$ and $P=0.038$), while TNF-alpha levels were increased significantly in both groups ($P=0.016$ and $P=0.014$; respectively). Statistical analysis revealed that testosterone treatment prior to stent implantation attenuated IL-6 and hs-CRP levels significantly ($P=0.042$ and $P=0.043$; respectively). CONCLUSIONS: The present study shows that 3 weeks testosterone treatment prior to intracoronary stenting results in a significant suppression in hs-CRP and IL-6 levels after the stent implantation.

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Interleukin-6 -174 G/C promoter polymorphism and effects of fenofibrate and simvastatin on inflammatory markers in hypercholesterolemic patients.

To evaluate whether the interleukin-6 (IL-6) -174 G/C polymorphism might alter the effects of micronized fenofibrate or simvastatin therapy on inflammatory markers, we measured IL-6, C-reactive protein, CD40 ligand, adhesion molecules, P-selectin and monocyte chemoattractant protein-1 in hypercholesterolemic patients both before and after a 30-day treatment. Serum IL-6 levels were significantly higher in patients with the GC or CC genotypes ($P=0.04$). The presence of the C allele was associated with greater absolute reduction of IL-6 levels.

(P=0.04) following fenofibrate treatment. There was no significant association between the -174 G/C IL-6 polymorphism and the effects of simvastatin treatment. A relationship between the -174 G/C IL-6 polymorphism and the anti-inflammatory action of fenofibrate reported might be useful in the optimization of the treatment regimen in patients receiving this class of drugs.

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Diet and exercise reduce low-grade inflammation and macrophage infiltration in adipose tissue but not in skeletal muscle in severely obese subjects.

Obesity is associated with low-grade inflammation, insulin resistance, type 2 diabetes, and cardiovascular disease. This study investigated the effect of a 15-wk lifestyle intervention (hypocaloric diet and daily exercise) on inflammatory markers in plasma, adipose tissue (AT), and skeletal muscle (SM) in 27 severely obese subjects (mean body mass index: 45.8 kg/m²). Plasma samples, subcutaneous abdominal AT biopsies, and vastus lateralis SM biopsies were obtained before and after the intervention and analyzed by ELISA and RT-PCR. The intervention reduced body weight (P < 0.001) and increased insulin sensitivity (homeostasis model assessment; P < 0.05). Plasma adiponectin (P < 0.001) increased, and C-reactive protein (P < 0.05), IL-6 (P < 0.01), IL-8 (P < 0.05), and monocyte chemoattractant protein-1 (P < 0.01) decreased. AT inflammation was reduced, determined from an increased mRNA expression of adiponectin (P < 0.001) and a decreased expression of macrophage-specific markers (CD14, CD68), IL-6, IL-8, and tumor necrosis factor-alpha (P < 0.01). After adjusting for macrophage infiltration in AT, only IL-6 mRNA was decreased (P < 0.05). Only very low levels of inflammatory markers were found in SM. The intervention had no effect on adiponectin receptor 1 and 2 mRNA in AT or SM. Thus hypocaloric diet and increased physical activity improved insulin sensitivity and reduced low-grade inflammation. Markers of inflammation were particularly reduced in AT, whereas SM does not contribute to this attenuation of whole body inflammation.

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Endurance training reduces circulating inflammatory markers in persons at risk of coronary events: impact on plaque stabilization?

Inflammatory pathways are involved in destabilization of atherosclerotic plaques. We assessed the hypothesis that endurance training decreases circulating concentrations of inflammatory markers in persons with coronary artery disease (CAD) and cardiovascular risk factors (CVRFs). Thirty-two subjects with CAD and/or CVRFs joined a 12-week supervised endurance training. We found a significant decrease of the chemokines interleukin (IL)-8 (pre: 3.9+/-0.6, change: -1.2+/-0.4 pg/ml, -21% p=0.002) and monocyte chemoattractant protein-1 (pre: 213+/-9, change: -20.4+/-8.2 pg/ml, -5% p=0.03). Diabetes mellitus (DM) significantly influenced changes of IL-8 (p=0.002). IL-8 substantially dropped by 39% in diabetics. Moreover, matrix metalloproteinase-9 (MMP-9) highly significantly decreased in response to training (pre: 750+/-98, change: -278+/-77 ng/ml, -18% p=0.005). Exercise-induced changes of MMP-9 were influenced by concomitant use of statins (p=0.038). We observed a particularly strong MMP-9 reduction of 44% in patients treated with statins. Acute phase reactants IL-6 (pre: 1.7+/-0.3, change: +0.25+/-0.7 pg/ml, +4% p=0.58) and high sensitivity C-reactive protein (pre: 2.1+/-0.5, change: -0.25+/-0.4 mg/l, -9% p=0.54) did not change in response to training. In conclusion, endurance training decreased circulating chemokines and MMP-9, which may in part explain its beneficial effect on coronary risk. Patients with DM or treated with statins because of hypercholesterolemia may particularly take advantage.

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Changes of plasma inflammatory markers after withdrawal of statin therapy in patients with hyperlipidemia.

BACKGROUND: Atherosclerosis has been considered to be an inflammatory process. In addition to its lipid-lowering properties, statin has been shown to decrease the concentrations of inflammatory markers resulting in reduction of cardiovascular events. Emerging data suggest that withdrawal of statin might be associated with increased cardiac events. The mechanism for this phenomenon, however, is still unclear. We investigated whether acute termination of statin treatment could result in rebound of inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6), in patients with hyperlipidemia. METHODS: Seventeen patients (11 men and 6 women, mean age 51+/-7 years) with hyperlipidemia were given 40

mg/day of pravastatin for 6 weeks. The concentrations of plasma CRP and IL-6 were evaluated before receiving the statin therapy, immediately after 6 weeks of pravastatin therapy, and at days 1, 3 and 7 after withdrawal of pravastatin therapy. The lipid profile was also evaluated at baseline, 6 weeks of therapy, and at day 7 after terminating pravastatin. **RESULTS:** Pravastatin therapy induced significant reductions in total cholesterol (TC, 6.88+/-0.36 vs. 5.27+/-0.23 mmol/l, p<0.01), low-density lipoprotein (LDL) cholesterol (4.28+/-0.25 vs. 3.06+/-0.14 mmol/l, p<0.01), CRP (0.28+/-0.16 vs. 0.20+/-0.08 mg/l, p<0.01), and IL-6 (8.4+/-0.6 vs. 6.7+/-0.4 pg/dl, p<0.01). Although the TC and LDL-cholesterol did not change during the 7-day period after withdrawal of pravastatin therapy, the concentrations of CRP and IL-6 increased at day 3 (CRP: 0.20+/-0.08 vs. 0.27+/-0.12 mg/l, and IL-6: 6.7+/-0.4 vs. 7.7+/-0.6 pg/dl, p<0.05 respectively) and at day 7 (CRP: 0.20+/-0.08 vs. 0.30+/-0.14 mg/l, and IL-6: 6.7+/-0.4 vs. 8.7+/-0.8 pg/dl, p<0.01 respectively) after withdrawal of pravastatin therapy. No correlation between increase of CRP as well as IL-6 and small changes of LDL-cholesterol concentrations was found after withdrawal of pravastatin therapy at day 7 (r=-0.021 and r=-0.044 respectively, p>0.05 respectively). **CONCLUSIONS:** 6 weeks after pravastatin therapy could significantly modify the lipid profile and decrease the inflammatory markers including CRP and IL-6 in patients with hyperlipidemia. Moreover, statin therapy discontinuation could induce a rebound phenomenon of inflammatory response representing an increase in some inflammatory markers, which is independent of changes of lipid parameters.

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The decrease in C-reactive protein concentration after diet and physical activity induced weight reduction is associated with changes in plasma lipids, but not interleukin-6 or adiponectin. Subclinical inflammation is a risk factor for cardiovascular disease. The mechanisms underlying increased levels of inflammatory markers and their changes in response to weight loss are not fully understood yet. It has been proposed that elevated concentrations of C-reactive protein (CRP) are mediated by cytokines produced in adipose tissue. We investigated the changes in circulating CRP after weight reduction, in relation to parameters relevant to the metabolic syndrome. Forty 25- to 35-year-old obese female volunteers participated in an intervention program of dietary education and supervised physical activity for a period of 9 weeks. Anthropological parameters and biochemical measurements (high-sensitivity CRP [hsCRP], plasma lipoproteins, interleukin 6 [IL-6], adiponectin) were analyzed before and after the intervention. Body mass index decreased by more than 7% from 31.5 +/- 4.1 to 29.1 +/- 3.9. Plasma free fatty acid (FFA) concentrations decreased by 30% high-density lipoprotein cholesterol increased by 8% and fasting insulin concentrations decreased by 15%. There were no significant changes in either low-density lipoprotein cholesterol or triacylglycerol concentrations. Subcutaneous and visceral adipose tissue mass decreased by 12% and 18%. High-sensitivity CRP concentrations decreased by 30% however, mean plasma IL-6 and adiponectin concentrations remained unchanged. In linear regression analysis, the changes in plasma hsCRP concentrations were associated with baseline hsCRP concentration, change in triacylglycerols and FFA concentrations, and in waist circumference. The decrease in hsCRP concentration after weight reduction does not appear to be mediated by decreases in circulating IL-6 or adiponectin concentrations; however, change in hsCRP concentration is related to changes in waist circumference and lipid metabolism reflected by plasma triacylglycerol and FFA levels.

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Effects of rosiglitazone on lipids, adipokines, and inflammatory markers in nondiabetic patients with low high-density lipoprotein cholesterol and metabolic syndrome.

BACKGROUND: PPAR-gamma agonists improve insulin sensitivity and glycemic control in type 2 diabetes and may reduce atherosclerosis progression. Thus, PPAR-gamma agonists may be an effective therapy for metabolic syndrome. However, the full spectrum of potentially antiatherogenic mechanisms of PPAR-gamma agonists have not been fully tested in nondiabetic patients with metabolic syndrome. **METHODS AND RESULTS:** We performed a prospective, double-blinded, placebo-controlled study of 60 nondiabetic subjects with low high-density lipoprotein cholesterol (HDL-C) level and metabolic syndrome to rosiglitazone 8 mg daily or placebo for 12 weeks. We found no significant effect of rosiglitazone on HDL-C (+5.5% versus +5.8% P=0.89), and an increase in total cholesterol (+8% versus -1% P=0.03). Nevertheless, rosiglitazone significantly increased adiponectin (+168% versus +25% P<0.001), and lowered resistin (-6% versus +4% P=0.009), C-reactive

protein (-32% versus +36% P=0.002), interleukin (IL)-6 (-22% versus +4% P<0.001), and soluble tumor-necrosis factor- α receptor-2 (-5% versus +7% P<0.001). CONCLUSIONS: These findings suggest that rosiglitazone, presumably through its PPAR-gamma agonist properties, has direct effects on inflammatory markers and adipokines in the absence of favorable lipid effects. These findings may help explain the mechanism underlying the possible antiatherosclerotic effects of rosiglitazone.

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In vivo and in vitro effects of simvastatin on inflammatory markers in pre-dialysis patients.

BACKGROUND: The beneficial effects of statins in reducing cardiovascular events have been attributed predominantly to their lipid-lowering effects, recent studies suggest that these effects might be due to their anti-inflammatory properties. We here investigate the in vivo and in vitro effects of simvastatin on cytokine production in pre-dialysis chronic renal failure patients. METHODS: Our clinical study has been designed as a randomized double-blind placebo controlled study. A total of 55 chronic kidney disease (CKD) patients at stages 3 and 4 (mean creatinine clearance 45 ml/min, range 15-60) were randomly assigned to receive simvastatin 40 mg/day or placebo, added to their ongoing treatment, for 6 months. Blood samples were obtained at baseline, and after 3 and 6 months of observation for the determination of lipids, inflammatory markers and renal function. For the in vitro studies, the effect of increasing doses of simvastatin on cytokine production [namely interleukin (IL)-6 and IL-8] in human cultured monocytes from 10 healthy subjects (HS) and 15 CKD patients stimulated by lipopolysaccharide (LPS) was investigated. RESULTS: A significant reduction in total cholesterol from 221+/-44 mg/dl to 184+/-41 mg/dl (3 months) and to 186+/-39 mg/dl (6 months) (P<0.02) and low-density lipoprotein cholesterol from 139+/-40 mg/dl to 104+/-29 mg/dl (3 months) and to 100+/-31 mg/dl (6 months) (P<0.001) was observed in the 28 patients treated with simvastatin. In this group, C-reactive protein (CRP) levels significantly decreased from 2.6 mg/l [interquartile range (IQR) 4.9] to 2.0 mg/l (IQR 1.9) (P = 0.03) at 6 months (P<0.05). A parallel reduction of IL-6 levels from 5.1 pg/ml (IQR 3.8) to 3.5 pg/ml (IQR 3.1) (P = 0.001) at 6 months was also observed. No significant reduction in inflammatory markers [CRP from 5.1 mg/l (IQR 1.9) to 5.4 mg/l (IQR 1.3) (P = NS) at 6 months] or plasma lipids [LDL-cholesterol from 127+/-32 mg/dl to 131+/-21 mg/dl (6 months)] was observed in the 27 patients of the placebo group. In the in vitro studies, the average value for cell-associated IL-6 and IL-8 was higher in CKD (155+/-95 pg/ml monocytes for IL-6 and 722+/-921 pg/ml monocytes for IL-8) vs HS (137+/-87 pg/ml monocytes and 186+/-125 pg/ml monocytes) (P<0.01) and was not affected by simvastatin alone. LPS resulted in a significant increase in cytokine production (IL-6: 1954+/-321 pg/ml monocytes for CKD and 1451+/-237 pg/ml monocytes for HS; P<0.001); the simultaneous addition of increasing doses of simvastatin to these cultures induced a dose-dependent inhibition of IL-6 and IL-8 production in stimulated peripheral blood mononuclear cells in all groups. CONCLUSIONS: These results indicate that simvastatin in commonly used doses has an in vitro and in vivo anti-inflammatory effect in CKD patients, and may play an important role in counteracting the mechanisms involved on the pathogenesis of cardiovascular disease.

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CRP reduction following gastric bypass surgery is most pronounced in insulin-sensitive subjects.

OBJECTIVE: Obesity is frequently associated with insulin resistance, dyslipidemia, hypertension and an increased risk of cardiovascular disease, reflected in elevated markers of inflammation, in particular C-reactive protein (CRP). To what extent the insulin resistance or the obesity per se contributes to increased CRP levels is unclear. In morbidly obese patients, gastric bypass surgery causes marked changes in body weight and improves metabolism thereby providing informative material for studies on the regulation of inflammatory markers. DESIGN: Prospective, surgical intervention study of inflammatory markers in morbidly obese subjects. SUBJECTS: In total, 66 obese subjects with mean age 39 y and mean body mass index (BM) 45 kg/m² were studied prior to and 6 and 12 months following Roux-en-Y gastric bypass (RYGBP) surgery. MEASUREMENTS: Serum concentrations of high sensitivity CRP, serum amyloid A (SAA) and interleukin-6 (IL-6), as well as markers of glucose and lipid metabolism. RESULTS: Prior to surgery, CRP levels were elevated compared to the reference range of healthy, normal-weight subjects. CRP correlated with insulin sensitivity, as reflected by the homeostatic model assessment (HOMA) index, but not BM, when corrected for age and gender. Surgery reduced BM from 45 to 31 kg/m²

and lowered CRP, SAA and IL-6 levels by 82, 57 and 50% respectively, at 12 months. The reduction in CRP was inversely related to HOMA at baseline independently of the change in body weight ($r=-0.36$, $P=0.005$). At 12 months, 140 and 40% reductions in CRP were seen in subjects with $HOMA < 4$ (insulin sensitive) and $HOMA > 9$ (insulin resistant) despite similar reductions in BM. Reductions in SAA and IL-6 tended to parallel the changes in CRP, but were less informative. CONCLUSION: In morbidly obese subjects, gastric bypass surgery lowers energy intake, reduces inflammatory markers and improves insulin sensitivity. Despite a marked reduction in body weight, only a small effect on CRP levels was seen in insulin-resistant patients, indicating that flexibility of circulating CRP levels is primarily dependent upon insulin sensitivity rather than energy supply.

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The effect of orlistat-induced weight loss on interleukin-6 and C-reactive protein levels in obese subjects.

OBJECTIVE: Inflammation plays a major role in the pathogenesis of atherosclerosis. Obesity is an independent risk factor for cardiovascular disease, which may be mediated by increased secretion of proinflammatory cytokines by adipose tissue. The aim of this study is to investigate changes in the inflammatory markers interleukin-6 (IL-6) and high-sensitivity C-reactive protein (hs-CRP) during weight reduction with orlistat treatment in obese patients.

METHODS AND RESULTS: Thirty-six obese (BM: $36.1 \pm 3.4 \text{ kg/m}^2$) and 11 non-obese (BM: $22.9 \pm 1.7 \text{ kg/m}^2$) subjects were studied. IL-6 and hs-CRP levels were evaluated at baseline. In obese subjects after treatment of orlistat 120 mg three times daily for 6 months, IL-6 and hs-CRP levels were repeated. Levels of circulating IL-6 ($p < 0.05$) and hs-CRP ($p < 0.01$) were significantly higher in the obese group than in the non-obese group. Plasma IL-6 ($r = 0.29$ and $p < 0.05$) and CRP ($r = 0.35$ and $p < 0.05$) concentrations correlated positively with the level of obesity assessed by BM at baseline. After 6 months of orlistat treatment in obese subjects, the mean weight of the patients decreased by 6.8 kg, the BM by 3.2 kg/m^2 . Compared with baseline, weight loss was associated with significant reductions of IL-6 ($p < 0.001$) and hs-CRP ($p < 0.001$) levels. CONCLUSION: In summary plasma IL-6 and hs-CRP levels were increased in obese patients. Orlistat-induced weight reduction was associated with decreasing levels of both IL-6 and hs-CRP in obese subjects. Because inflammatory mediators may be directly involved in atherosogenesis, this would suggest that interventions to reduce IL-6 and CRP levels could be cardioprotective.

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Effects of bezafibrate on lipoprotein subclasses and inflammatory markers in patients with hypertriglyceridemia--a nuclear magnetic resonance study.

BACKGROUND: Hypertriglyceridemia is often associated with elevated remnants, small dense LDL and decreased HDL-cholesterol (C). The objective of this study was to investigate the efficacy of bezafibrate on lipoprotein subfractions profile and inflammation markers in patients with hypertriglyceridemia. METHODS: Twenty-four hypertriglyceridemic subjects took bezafibrate, 400 mg daily, for 4 weeks. Lipoprotein subclasses were measured by nuclear magnetic resonance (NMR) spectroscopy. Inflammation markers including C-reactive protein (CRP), interleukin-6 (IL-6) and monocyte chemoattractant protein-1 (MCP-1) were also determined. RESULTS: Bezafibrate lowered triglyceride (TG) by 59% and increased HDL-C by 20%. NMR analysis revealed that bezafibrate lowered large TG-rich lipoproteins and LDL by 81% and 46%, respectively. Small LDL was selectively decreased by 53% with increase in large to intermediate LDL, thus altering the LDL distribution towards the larger particles (mean diameter 19.9 to 20.7 nm $p = 0.0001$). Small (HDL1) and intermediate (HDL3) HDL significantly increased by 168% and 70%, whereby resulting in a significant reduction of the mean HDL particle size from 9.0 to 8.7 nm ($p = 0.026$). None of inflammation makers showed significant change by bezafibrate. CONCLUSIONS: Bezafibrate effectively ameliorates atherosogenic dyslipidemia by reducing remnants and small LDL as well as by increasing HDL particles in hypertriglyceridemic subjects.

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Effect of preexisting statin use on expression of C-reactive protein, adhesion molecules, interleukin-6, and anti oxidized low-density lipoprotein antibody in patients with unstable angina undergoing coronary stenting.

BACKGROUND: Statins are believed to reduce coronary heart disease by mechanisms in addition to their well-known cholesterol lowering effect. **HYPOTHESIS:** We studied the effect of statins on expression of C-reactive protein (CRP), interleukin-6 (IL-6), adhesion molecules, and anti oxidized low-density lipoprotein antibody (anti-oxLDL Ab) in patients with unstable angina (Braunwald class IIb or IIIb) undergoing coronary stenting. **METHODS:** Consecutive 50 patients with unstable angina were included in the study. We classified the study subjects as patients using statins (Group A, n=20, men 10, mean age 62 years) and patients not using statins (Group B, n=30, men 15, mean age 60 years). **RESULTS:** Baseline levels of inflammatory markers were similar in the two groups. However, 24 h after coronary stenting, serum levels of CRP (2.00 vs. 4.63 mg/l, p < 0.05), intercellular adhesion molecule-1 (ICAM-1) (217 vs. 261 ng/ml, p < 0.01), and anti-oxLDL Ab (8.97 vs. 12.96 U/ml, p < 0.05) were significantly higher in Group B than in Group A. Furthermore, 72 h after coronary stenting, serum levels of CRP (3.00 vs. 5.50 mg/l, p < 0.01) and ICAM-1 (222 vs. 277 ng/ml, p < 0.05) were significantly higher in Group B than in Group A. **CONCLUSIONS:** Preexisting statin therapy plays a role in reducing the serum levels of CRP, ICAM-1, and anti-oxLDL Ab after coronary stenting in patients with unstable angina. These data support an anti-inflammatory or plaque-stabilizing effect of statin therapy.

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Glycation and inflammatory markers in patients on treatment with PMMA-based protein-leaking dialyzers.

BACKGROUND: High-molecular-weight solutes such as glycation and oxidation protein products are putative proinflammatory mediators found in the uremic blood. The elimination of these and other large solutes by protein-leaking dialyzers (PLD) might help to correct the inflammatory status of maintenance hemodialysis (HD) patients. **METHODS:** Two matched groups of 13 standard 3 times/week HD patients were treated for 6 months with PMMA-based PLD and non-protein-leaking dialyzers (NPLD), respectively. At baseline, 1, 3, and 6 months, we measured the blood levels of the inflammatory cytokines IL-1beta, TNF-alpha, IL-6, the acute-phase protein C-reactive protein (CRP), the adhesion molecules ICAM-1, VCAM-1, and selectin-E, the chemotaxis factors MCP-1, and the glycation and oxidation protein end products pentosidine, protein carbonyls, and AOPP. **RESULTS:** In all the patients at baseline, pre-HD levels of glycation and oxidation protein markers, and inflammatory parameters were significantly higher than in healthy control subjects (P < 0.01 or greater). After 6 months, in the group on treatment with PLD, but not in that on NPLD, there was a significant decrease (P < 0.05 or greater) of pre-HD values of total pentosidine (mainly represented by pentosidine in serum albumin; -43%, protein carbonyls (-42%, AOPP (-38%, and the inflammatory cytokines IL-1beta (-49%, IL-6 (-39%, and TNF-alpha (-20%, while IL-10 and TNF-gamma increased by 67% and 37% respectively. Proinflammatory cytokines, and particularly IL-6, showed a positive correlation with the levels of circulating pentosidine. Proteinuria was not significantly modified at the end of the study in both the groups. **CONCLUSION:** The results in this pilot study show that the removal of large solutes by PLD can improve some indices of chronic inflammation in HD patients. Further studies are required to determine the relevance of the individual solutes removed with PLD as proinflammatory mediators in the uremic environment.

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Weight reduction, but not a moderate intake of fish oil, lowers concentrations of inflammatory markers and PAI-1 antigen in obese men during the fasting and postprandial state.

BACKGROUND: In obese subjects, chronic low-grade inflammation contributes to an increased risk of metabolic abnormalities, which are reversed by weight loss. Sustained weight loss, however, is difficult to achieve and more insight into dietary approaches on anti-inflammatory responses in obese subjects is needed. In this respect, fish oil deserves attention. **MATERIAL AND METHODS:** Eleven obese men (BM: 30-35 kg m(-2)) received daily fish oil (1.35 g n-3 fatty acids) or placebo capsules in random order for 6 weeks. Eight subjects continued with a weight reduction study that lasted 8 weeks. Mean weight loss was 9.4 kg. At the end of each experimental period a postprandial study was performed. **RESULTS:** Relative to fasting concentrations, interleukin-6 (IL-6) levels increased by 75% 2 h and by 118% 4 h after the meal (P < 0.001), when subjects consumed the control capsules. In contrast, C-reactive protein (CRP) concentrations decreased slightly by 0.7% and 6.6% (P = 0.046), and those of plasminogen activator inhibitor-1 (PAI-1) antigen by, respectively, 26% and 53% (P < 0.001). Tumour necrosis factor-alpha (TNF-alpha; P = 0.330) and soluble TNF-receptor concentrations (sTNF-R55 and sTNF-R75; P = 0.451 and P = 0.108, respectively) did not change.

Changes relative to fasting concentrations were not significantly affected by either fish oil or weight reduction. Absolute IL-6, C-RP, sTNF-R55, sTNF-R75, and PAI-1 antigen concentrations, however, were consistently lower after weight reduction, but not after fish oil consumption. CONCLUSION: For slightly obese subjects a moderate intake of fish oil does not have the same favourable effects on markers for a low-grade inflammatory state as weight reduction.

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Effect of liposuction on insulin resistance and vascular inflammatory markers in obese women.

Liposuction is one of the more common elective surgical procedures in the US and is supposed to be on the increase. There are no reported studies specifically addressing the metabolic sequelae of liposuction in obesity. The aim of the present study was to investigate the role of large-volume liposuction on insulin resistance and circulating inflammatory markers in obese people. Thirty healthy premenopausal obese (body mass index (BM) from 30 to 45) and 30 age-matched normal weight (BM <25) women were studied. In obese women, insulin sensitivity, as measured by the Homeostasis Model Assessment (HOMA=fasting plasma glucose x fasting serum insulin divided by 25), as well as serum adiponectin, the novel adipocytokine with insulin sensitising properties, were significantly lower, as compared with nonobese women ($p<0.01$), indicating insulin resistance; on the contrary, serum concentrations of the proinflammatory cytokines IL-6, IL-18 and TNF-alpha, as well as the sensitive marker of inflammation C-reactive protein, were significantly higher ($p<0.01$). All obese women were submitted to a single large volume liposuction (superwet technique): the mean aspirate volume was 3540 ml (range 2550-4670), corresponding to a net lipid loss of 2.7+/-0.7 kg (mean+/-SD). After six months of stable body weight after liposuction, women were less insulin resistant ($p<0.05$), had reduced concentrations of IL-6, IL-18, TNF-alpha and CRP ($p<0.05$ -0.02), and increased serum levels of adiponectin ($p<0.02$) and HDL-cholesterol ($p<0.05$). There was a significant correlation between the amount of fat aspirate and changes in HOMA ($r=0.28$, $p<0.05$), TNF-alpha ($r=0.31$, $p<0.02$), and adiponectin ($r=0.34$, $p<0.02$), as well as between the decrease in TNF-alpha and the increase in adiponectin after the surgical procedure ($r=-0.45$, $p<0.01$). Our study demonstrates that liposuction is safe and free of metabolic sequelae in obese women, pending a careful screening of the patient. Moreover, it is associated with amelioration of insulin resistance and reduced circulating markers of vascular inflammation which may help obese subjects to reduce their cardiovascular risk.

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Periodontitis and systemic inflammation: control of the local infection is associated with a reduction in serum inflammatory markers.

Severe periodontitis is associated with elevated inflammatory markers in otherwise healthy populations. However, the nature of this association has not been determined. Our aim was to assess whether the degree of response to periodontal therapy was associated with changes in serological markers of systemic inflammation. Ninety-four systemically healthy subjects with severe generalized periodontitis participated in a prospective six-month blind intervention trial. Periodontal parameters and inflammatory markers [C-reactive Protein (CRP) and Interleukin-6 (IL-6)] were evaluated prior to and 2 and 6 mos after delivery of standard non-surgical periodontal therapy. Six months after treatment, significant reductions in serum IL-6 ($p < 0.001$, median decrease 0.2 ng/L, 95% CI 0.1-0.4 ng/L) and CRP ($p < 0.0001$, median decrease 0.5 mg/L, 95% CI 0.4-0.7) were observed. Decreases in inflammatory markers were significant in subjects with above average clinical response to periodontal therapy after correction for possible confounders. Periodontitis may add to the systemic inflammatory burden of affected individuals.

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Effect of eicosapentaenoic acid and docosahexaenoic acid on oxidative stress and inflammatory markers in treated-hypertensive type 2 diabetic subjects.

n-3 fatty acids reduce the risk of cardiovascular disease via a number of possible mechanisms. Despite this, there has been concern that these fatty acids may increase lipid peroxidation. The data *in vivo* are inconclusive, due in part to limitations in the methodologies. In this regard, the measurement of F2-isoprostanes provides a reliable assessment of *in vivo* lipid peroxidation and oxidant stress. This study aimed to

assess the effects of supplementation with purified eicosapentaenoic acid (EPA) or docosahexaenoic acid (DHA), the two major n-3 fatty acids, on urinary F2-isoprostanes and markers of inflammation, in type 2 diabetic patients. In a double-blind, placebo controlled trial of parallel design, 59 nonsmoking, treated-hypertensive, type 2 diabetic subjects, were randomized to 4 g daily of purified EPA, DHA, or olive oil for 6 weeks, while maintaining their usual diet. F2-isoprostanes, measured using gas chromatography-mass spectrometry in 24 h urines and C-reactive protein (CRP), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-alpha), were measured before and after intervention. Thirty-nine men and 12 women aged 61.2 +/- 1.2 years, with body mass index (BM), 29.5 +/- 0.5 kg/m²; 24 h blood pressure, 138/73 mmHg; HbA1c, 7.3 +/- 0.1% and fasting glucose, 7.9 +/- 0.2 mmol/l completed the intervention. Baseline urinary F2-isoprostanes were positively associated with HbA1c (p= 0.011) and fasting glucose (p= 0.032). Relative to the olive oil group, post intervention urinary F2-isoprostanes were decreased 19% by EPA (p= 0.017) and 20% by DHA (p= 0.014). There were no significant changes in CRP, IL-6, and TNF-alpha following EPA or DHA supplementation. In regression analysis, Delta F2-isoprostanes were positively associated with Delta HbA1c (p= 0.007) independent of treatment group; and with Delta TNF-alpha (p= 0.034) independent of age, gender, BM, and treatment group. There were no associations with Delta CRP or Delta IL-6. This study is the first report demonstrating that either EPA or DHA reduce in vivo oxidant stress without changing markers of inflammation, in treated hypertensive, type 2 diabetic subjects.

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High-dose atorvastatin enhances the decline in inflammatory markers in patients with acute coronary syndromes in the M RACL study.

BACKGROUND: Inflammation promotes acute coronary syndromes and ensuing clinical complications. Although statins reduce inflammatory markers in asymptomatic adults or in patients with stable angina, the effect of statins on the markedly heightened inflammation in patients with acute coronary syndromes is unknown. **METHODS AND RESULTS:** We measured C-reactive protein (CRP), serum amyloid A (SAA), and interleukin 6 (IL-6) in 2402 subjects enrolled the Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering (M RACL) study. Subjects with unstable angina or non-Q wave myocardial infarction were randomized to atorvastatin 80 mg/d or placebo within 24 to 96 hours of hospital admission and treated for 16 weeks. The effect of treatment on inflammatory markers was assessed by ANCOVA after adjustment for presenting syndrome, country, and initial level of marker. All 3 markers were markedly elevated at randomization and declined over the 16 weeks in both treatment groups. Compared with placebo, atorvastatin significantly reduced CRP, -83% (95% CI, -84% -81% versus -74% (95% CI, -75% -71% (P<0.0001) and SAA, -80% (95% CI, -82% -78% versus -77% (-79% -75% (P=0.006) but not IL-6, -55% (95% CI, -57% -53% versus -53% (95% CI, -55% -51% (P=0.3). Reductions in CRP and SAA were observed in patients with unstable angina and non-Q wave myocardial infarction, with initial LDL cholesterol <3.2 or > or =3.2 mmol/L (125 mg/dL), age > or =65 or <65 years, and in men and women. By 16 weeks, CRP was 34% lower with atorvastatin than with placebo. **CONCLUSIONS:** High-dose atorvastatin potentiated the decline in inflammation in patients with acute coronary syndromes. This supports the value of early statin therapy in these patients.

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Effect of weight loss and lifestyle changes on vascular inflammatory markers in obese women: a randomized trial.

CONTEXT: Obesity is an independent risk factor for cardiovascular disease, which may be mediated by increased secretion of proinflammatory cytokines by adipose tissue. **OBJECTIVE:** To determine the effect of a program of changes in lifestyle designed to obtain a sustained reduction of body weight on markers of systemic vascular inflammation and insulin resistance. **DESIGN AND SETTING:** Randomized single-blind trial conducted from February 1999 to February 2002 at a university hospital in Italy. **PATIENTS:** One hundred twenty premenopausal obese women (body mass index > or =30) aged 20 to 46 years without diabetes, hypertension, or hyperlipidemia. **INTERVENTIONS:** The 60 women randomly assigned to the intervention group received detailed advice about how to achieve a reduction of weight of 10% or more through a low-energy Mediterranean-style diet and increased physical activity. The control group (n = 60) was given general information about healthy food choices and exercise. **MAIN OUTCOME MEASURES:** Lipid and glucose intake; blood pressure; homeostatic model assessment of insulin sensitivity; and circulating levels of interleukin 6 (IL-6), interleukin 18 (IL-18), C-reactive protein (CRP), and adiponectin. **RESULTS:** After 2

years, women in the intervention group consumed more foods rich in complex carbohydrates (9% corrected difference; $P < .001$), monounsaturated fat (2% $P = .009$), and fiber (7 g/d; $P < .001$); had a lower ratio of omega-6 to omega-3 fatty acids (-5; $P < .001$); and had lower energy (-310 kcal/d; $P < .001$), saturated fat (-3.5%; $P = .007$), and cholesterol intake (-92 mg/d; $P < .001$) than controls. Body mass index decreased more in the intervention group than in controls (-4.2; $P < .001$), as did serum concentrations of IL-6 (-1.1 pg/mL; $P = .009$), IL-18 (-57 pg/mL; $P = .02$), and CRP (-1.6 mg/L; $P = .008$), while adiponectin levels increased significantly (2.2 microg/mL; $P = .01$). In multivariate analyses, changes in free fatty acids ($P = .008$), IL-6 ($P = .02$), and adiponectin ($P = .007$) levels were independently associated with changes in insulin sensitivity. CONCLUSION: In this study, a multidisciplinary program aimed to reduce body weight in obese women through lifestyle changes was associated with a reduction in markers of vascular inflammation and insulin resistance.

? logout

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\$6.00 25 Type(s) in Format 4 (UDF)
\$6.00 25 Types
\$14.42 Estimated cost File155
\$1.60 TELNET
\$16.02 Estimated cost this search
\$16.04 Estimated total session cost 2.777 Dial Units

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